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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/388,899	09/02/99	HOUWEN	B 10690/T/B/A

HM22/0731

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EXAMINER

GABEL, G

ART UNIT PAPER NUMBER

1641

8

DATE MAILED:

07/31/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application N .

09/388,899

Applicant(s)

HOUWEN ET AL.

Examiner

Gailene R. Gabel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 3/22/01 in Paper No. 8 is acknowledged and has been entered. Claims 1-11 have been amended. Currently, claims 1-11 are pending and under examination.

Oath/Declaration

2. Applicant's response with regards to the date of signing of the declaration by Applicant is noted. Such information can be deferred but will be required upon allowance of the application by the examiner.

Rejections Withdrawn

Claim Rejections - 35 USC § 112

3. In light of Applicant's amendment, the rejection of claims 1-11 under 35 U.S.C. 112, second paragraph, is hereby, withdrawn.

4. In light of Applicant's amendment, the rejection of claims 1, 3-4, and 7-10 under 35 U.S.C. 102(b) as being anticipated by Hubl et al. (Cytometry, 1997), is hereby, withdrawn.

5. In light of Applicant's amendment, the rejection of claims 1, 3, and 7-11 under 35 U.S.C. 102(b) as being anticipated by Jackson et al. (US 5,776,709), is hereby, withdrawn.

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6. In light of Applicant's amendment, the rejection of claim 11 under 35 U.S.C. 103(a) as being unpatentable over Hubl et al. (Cytometry, 1997) in view of McCarthy et al. (Journal of Immunological Methods, 1993), is hereby, withdrawn.

Rejections Maintained

Claim Rejections - 35 USC § 102/103

7. Claims 1-10 stand rejected under 35 U.S.C. 102(b) as being anticipated by Bowen et al. (Laboratory Hematology, 1997) for reason of record.
8. Claims 1-10 stand rejected under 35 U.S.C. 102(b) as being anticipated by Loken et al. (EP 0317516) for reason of record.
9. Claim 11 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Bowen et al. (Laboratory Hematology, 1997) in view of McCarthy et al. (Journal of Immunological Methods, 1993) for reason of record.

Response to Arguments

10. Applicant's arguments filed 3/22/01 have been fully considered but they are not persuasive.

A) Applicant argues that Bowen does not anticipate the claimed invention because Bowen fails to define granulocytic cells in different stages of maturity on the basis of fluorescent intensities from a first and a second or third antibody but rather categorize between mature and immature cells together.

Contrary to Applicant's argument, Bowen teaches classifying and counting leucocytes including differentiating between immature (abnormal) granulocytic populations via expressions of CD45 antigens by leucocytes and between CD16 and CD11b antigens by granulocytes using flow cytometric monoclonal antibody-based, three color immunofluorescence and light scatter technique. Bowen uses different labeled monoclonal antibodies specific thereto in identifying cell surface expressions for each population. Bowen teaches that immature and mature granulocytic populations are defined and separated from other leucocytes, i.e. agranulocytic cells such as blast, monocyte, and lymphocyte, on the basis of CD 45 fluorescence and side or orthogonal angle light scatter (SALS) – specifically, agranulocytic cells have lower SALS (see page 292, column 2- specifically, first full paragraph and page 294, column 1). Bowen teaches that different maturation levels of granulocytic populations can be defined by virtue of CD16 and CD11b antigenic expression and that in the course of granulocyte maturation, CD11b expression appears earlier in the left shift and prior to the expression of CD16, i.e. CD 11b is absent in promyelocytic stage but appears in early myelocytic stages whereas CD16 first appears in metamyelocytic ("more mature") stage and increases through mature segmented polymorphonuclear stages. Bowen, therefore, is said to inherently include all the elements required by the claimed invention.

B) Applicant argues that Loken fails to disclose classifying a defined group of neutrophilic cells within a defined group of granulocytic cells into groups of different degrees of maturity as required in claim 1.

In response, Loken indeed discloses classifying and counting populations hematopoietic cells including leucocytes. Loken discloses identifying all leucocytes using fluorochrome labeled anti-CD45 antibody. Loken further discloses identifying between maturational levels of granulocytes using labeled anti-CD16 and anti-CD11b antibodies which are used for their ability to distinguish between granulocytic myeloid maturation stages (see column 6, lines 11-15 and lines 38-47). Loken discloses assessment of granulocyte maturation levels using monoclonal antibodies including anti-CD16 and anti-CD11b in combination with anti-CD45 with fluorochrome labels having different emission spectra (see column 9, lines 1-2) and further separates granular from agranular cells by virtue of SALS which provides approximation of cellular granularity (see column 3 and 5). Loken, therefore, is said to inherently include all the elements required by the claimed invention.

C) Applicant further argues that Loken does not disclose distinguishing granulocytes from eosinophils.

In response, it is noted that the features upon which applicant relies (i.e., distinguishing granulocytes from eosinophils) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26

USPQ2d 1057 (Fed. Cir. 1993). Alternatively, eosinophils are granulocytes (containing granules) which should inherently be separated and distinguished in the early myelocytic stages with the rest of the neutrophilic cell population.

D) Applicant argues that McCarthy teaches away from removal of erythrocytes prior to staining and that available procedures affect the sample and are not desirable. Therefore, McCarthy lacks the requisite suggestion or motivation to obtain the claimed invention.

In response, Bowen stained a bone marrow sample using different labeled monoclonal antibodies then removed erythrocytes using Ortho Lyse. Bowen differs in failing to stain leucocytes after erythrocytes are removed from the hematological sample. McCarthy is incorporated therewith, only for teaching that peripheral blood neutrophils can optionally be separated from other cells, i.e. remove erythrocytes, prior to being labeled for flow cytometric analysis in 155, column 2.

One of ordinary skill in the art at the time of the instant invention would have reasonable expectation of success in separating leucocytes from erythrocytes using Ficoll-Hypaque and dextran sedimentation techniques such as taught by McCarthy prior to labeling for cytometric analysis such as taught Bowen because cellular separation or removal, including other manual separation methods, i.e. centrifugation to remove buffy coat containing leucocyte populations from the packed red cell population, is conventional and well-known in the art. An issue of when such a purification or

separation procedure is introduced into a method of flow cytometric analysis, i.e. before or after binding of a label to desired cells, is therefore an obvious design choice.

11. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

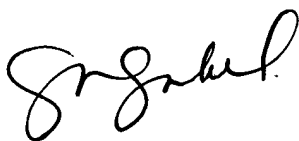
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday, 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for

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the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



grg
July 24, 2001



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

07/27/01